



09/856, 400

GfC

WILLIAMS, MORGAN & AMERSON, P.C.

10333 RICHMOND, STE. 1100, HOUSTON, TEXAS 77042
(713) 934-7000 FAX: (713) 934-7011

Danny L. Williams
Terry D. Morgan
J. Mike Amerson
Kenneth D. Goodman
Jeffrey A. Pyle
Jaison C. John
Ruben S. Bains

Shelley P.M. Fussey, Ph.D.*
Mark D. Moore, Ph.D.*
Raymund F. Eich, Ph.D.*
Daren C. Davis*
Mark W. Sincell, Ph.D.*


*Patent Agent

WRITER'S DIRECT DIAL:
713.934.4079

December 21, 2004

File: 4040.000300

**Certificate
JAN 03 2005
of Correction**

CERTIFICATE OF MAILING 37 C.F.R. § 1.8	
I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:	
December 21, 2004	
Date	Shelley P.M. Fussey

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RE: *U.S. Patent No. 6,824,761*; based on Application Serial No. 09/856,400;
Entitled "Anti-Asthmatic Combinations Comprising Surface Active Phospholipids"; Inventors: Hills et al.; Client Ref: CAH/TJH/4906US

Sir:

Enclosed are two originals of the form PTO-1050. An error of a minor nature is thereon corrected. The error on the title page is due to a Patent Office oversight.

Correction of the error in the document cited by the examiner, which needs to be marked *, is supported by the Office Action dated October 02, 2002 (copy attached).

A Certificate of Correction is requested under 35 U.S.C. § 254. Should any fee under 37 C.F.R. § 1.20(a) be required for any reason, the Director is authorized to deduct said fee from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4040.000300.

- 5 JAN 2005

WILLIAMS, MORGAN & AMERSON, P.C.

Commissioner for Patents

December 21, 2004

Page 2

Please date stamp and return the enclosed postcard evidencing receipt of these documents.

Respectfully submitted,

Williams, Morgan & Amerson, P.C.

Customer No. 23720



Shelley P.M. Fussey, Ph.D.

Reg. No. 39,458

Agent for Applicants

Encls.

UNITED STATES PATENT AND TRADEMARK OFFICE **CERTIFICATE OF CORRECTION**

PATENT NO. : 6,824,761 *B1*
 DATED : November 30, 2004
 INVENTOR(S) : Hills et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In title page, Section (56), right column, line 9, after "WO 96/19199 6/1996" please insert --*--.

MAILING ADDRESS OF SENDER:
 Shelley P.M. Fussey, Ph.D.
 WILLIAMS, MORGAN & AMERSON, P.C.
 10333 Richmond, Suite 1100
 Houston, Texas 77042

PATENT NO. 6,824,761
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5 JAN 2005



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,400	09/17/2001	Brian Andrew Hills	4040.000300	9184

7590

10/02/2002

Shelley P M Fussey
Williams Morgan & Amerson
7676 Hillmont Suite 250
Houston, TX 77040

EXAMINER

HAGHIGHATIAN, MINA

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 10/02/2002

T

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETING DEPT.

OCT 07 2002

WILLIAMS, MORGAN & AMERSON

Office Action Summary

Application No.

09/856,400

Applicant(s)

HILLS ET AL.

Examiner

Mina Haghighatian

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

4040.000300

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-35 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Resp to JA
DOCKETED
FOR 1-2-03
BY SM
CHK'D BY J

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:—

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radhakrishnan et al (4,895,719) in view of Mautone (5,306,483).

Radhakrishnan teaches method and apparatus for administering dehydrated liposomes by inhalation. Disclosed is a liposome-based aerosol system for delivering a drug, at a controlled release rate, via the respiratory tract. Two discoveries are made, first, rapid systemic uptake of drugs from the site of administration in the respiratory tract can be eliminated or greatly reduced by administering the drug in a predominantly liposome-encapsulated form. Secondly, it was found that the rate of release of a water-

Art Unit: 1616

soluble drug from a drug/liposome composition delivered to the respiratory tract can be modulated according to the acyl-chain composition of the phospholipids making up liposomes (col. 2, lines 55-68).

Radhakrishnan also teaches that administration of the β_2 -agonist metaproteranol sulfate(MPS) in liposomeal form via inhalation reduced initial plasma levels of the drug more than about 8 fold with respect to free drug, and that plasma levels remained substantially constant over a two hour period. Also disclosed is that β_2 -adrenoreceptor agonists, when administered in liposome-entrapped form at a therapeutic dose, produce significantly greater bronchodilation, over an extended time period, than is produced by the same amount of β_2 -agonist delivered to the respiratory tract in a free drug aerosol form (col. 3, lines 20-47).

Radhakrishnan discloses that the particles formed have a fine particle size, retain the majority of their originally encapsulated material, and are stable. The delivery device is a metered dose spray device designed to release a selected volume of the suspension in aerosolized form (col. 3, line 48 to col. 4, line 15).

Radhakrishnan teaches the effect of liposome lipid components on the rate of drug release in the respiratory tract, the combination of specific phospholipids and that the effect of lipid charge on drug release rates indicates that the addition of a negatively charged lipid, such as phosphatidylglycerol (PG) at a mole ratio of about 10%, produces a slight to moderate increase in efflux half life. Table 1 discloses some properties of phospholipids used in liposomes (col. 5, lines 5 to col. 6, line 68).

The pharmaceutically active agents suitable for the liposome preparations are listed in column 7, which include albuterol sulfate, terbutaline sulfate, atropine methyl nitrate, cromolyn sodium, beclomethasone, dexamethasone etc. The said preparations contain particles optimally less than about 5 microns (col. 8, lines 30-53).

Radhakrishnan does not teach the separate administration of components and lacks specific teachings on the weight ratios for the components.

Mautone teaches a process to prepare lipid crystalline figures in chloro or hydro fluorocarbon propellants or mixtures thereof for the aerosol delivery of therapeutically active substances. The acellular surface film of the lung, the so-called surfactant system, and the various phospholipids are described in columns 1 to 4. Also disclosed is that the vehicle system for the said invention can deliver for example 5 mg each of DPPC:CP, DPPC:PG or DPPC:CP:PG (200:1, 7:1 or 7:0.35:1, w/w, respectively), which when delivered quantitatively covers 100% of the airspace surface in the lungs of normal adults (col. 4, lines 3-33).

Mautone describes the process of preparing lipid crystals in combination with a therapeutically active substance comprising: preparing a mixture one or more lipids of the group of phospholipids known as phosphatidylcholines and one or more spreading agents, in powder form, and said therapeutically active substance and one or more fluorocarbon propellants (col. 5, lines 5-42). The major lipid component is the phospholipid 1,2dipalmitoyl phosphatidylcholin (DPPC) which is the most surface active of the phospholipids. Another minor lipid component that acts as a spreading agent for

Art Unit: 1616

the major component can be diacylphosphatidylglycerol (PG) (col. 6, lines 4-68).

Aerosolized drug delivery systems and the method of making them are described in examples I-VI. The administration of the aerosolized drug delivery system and the device are explained in columns 10 and 11.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the preparations of Radhakrishnan by adding the component ratios as taught by Mautone, and because Mautone teaches that the liposome preparations can be administered with or without a drug. Also because of the disclosed benefits of the lung surfactants in respiratory disorders and in carrying drugs into the lung. Furthermore, it would be a logical extension of the combined teachings to prepare the formulations as a combined product, such as a pack and to include patient instructions for proper administration and use.

Claims 1-2 and 6-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bystrom (WO9619199).

Bystrom teaches a proliposome powders for inhalation comprising in a single phase discrete particles of a biologically active component together with a lipid or mixture of lipids having a phase transition temperature of below 37 °C. the powder is particularly suitable for administration by inhalation (page 3, lines 16-22).

Potentially useful lipids may be of natural or synthetic lipids. These lipids are such as DPPC, DSPC, DMPC, DMPG, DPPG etc. Lipids of particular interest in the said

Art Unit: 1616

formulations are DPPC and/or DMPC. A mixture of DPPC and DMPC containing at least 10% (w/w) DMPC is preferred, for example 10-50% DMPC (page 4, line 16 to page 5, line 12).

Suitable active components include anti-inflammatory and bronchorelaxing drugs, antihistamines, leukotriene synthesis inhibitors, leukotriene antagonists, glucocorticosteroids, β_2 -agonists etc. The active component may also be a mixture of pharmaceutically active substances, for example, a mixture of a glucocortico-steroid with a bronchodilator (page 5, line 21 to page 6, line 10).

Where delivery by inhalation is desired, as much as possible of the proliposome powder of the present invention should consist of particles having a diameter of less than 10 microns, for example 0.01 to 10 microns or 0.1 to 5 microns (page 6, lines 27-30).

Bystrom also teaches that the proliposome powder of the present invention is useful for the local or systemic treatment of diseases and may be administered for example via the upper and lower respiratory tract. The proliposome powder for use in therapy, the use of the proliposome powder in the manufacture of a medicament for the treatment of diseases via the respiratory tract, and a method for the treatment of a patient in need of therapy, comprising administering to said patient a therapeutically effective amount of the said proliposome powder preparation. The proliposome powder preparation may be used in the treatment of inflammatory diseases in the respiratory tract, for example asthma, rhinitis, etc. Administration to the respiratory tract may be

Art Unit: 1616

effected using a dry powder inhaler or a pressurized aerosol inhaler (page 9, line 15 to page 10, line 11).

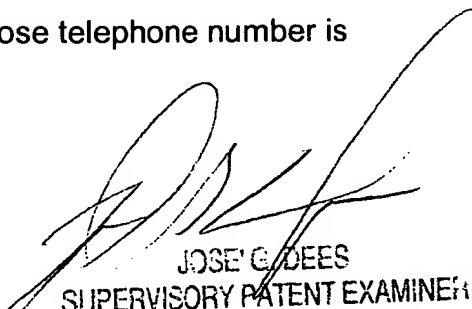
Although Bystrom does not specifically teach a combination product, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the preparations to a combined product because of the disclosed properties of the liposomes and their benefits in treating respiratory disorders and also the advantages of using liposomes as carriers for drug components.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
September 20, 2002


JOSE G. DEES
SUPERVISORY PATENT EXAMINER
1616

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,824,761
DATED : November 30, 2004
INVENTOR(S) : Hills et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In title page, Section (56), right column, line 9, after "WO 96/19199 6/1996" please insert --*--.

MAILING ADDRESS OF SENDER:
Shelley P.M. Fussey, Ph.D.
WILLIAMS, MORGAN & AMERSON, P.C.
10333 Richmond, Suite 1100
Houston, Texas 77042

PATENT NO. 6,824,761
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,400	09/17/2001	Brian Andrew Hills	4040.000300	9184

7590 10/02/2002

Shelley P M Fussey
Williams Morgan & Amerson
7676 Hillmont Suite 250
Houston, TX 77040

EXAMINER

HAGHIGHATIAN, MINA

ART UNIT	PAPER NUMBER
----------	--------------

1616

DATE MAILED: 10/02/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETING DEPT.

OCT 07 2002

WILLIAMS, MORGAN & AMERSON

Office Action Summary

Application No.

09/856,400

Applicant(s)

HILLS ET AL.

Examiner

Mina Haghghatian

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

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Status

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Resp to JA
DOCKETED
FOR 1-2-03
BY [Signature]
CHK'D BY [Signature]

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
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 - ☐ Certified copies of the priority documents have been received in Application No. ____.
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DETAILED ACTION

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Art Unit: 1616

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Bystrom teaches a proliposome powders for inhalation comprising in a single phase discrete particles of a biologically active component together with a lipid or mixture of lipids having a phase transition temperature of below 37 °C. the powder is particularly suitable for administration by inhalation (page 3, lines 16-22).

Potentially useful lipids may be of natural or synthetic lipids. These lipids are such as DPPC, DSPC, DMPC, DMPG, DPPG etc. Lipids of particular interest in the said

formulations are DPPC and/or DMPC. A mixture of DPPC and DMPC containing at least 10% (w/w) DMPC is preferred, for example 10-50% DMPC (page 4, line 16 to page 5, line 12).

Suitable active components include anti-inflammatory and bronchorelaxing drugs, antihistamines, leukotriene synthesis inhibitors, leukotriene antagonists, glucocorticosteroids, β_2 -agonists etc. The active component may also be a mixture of pharmaceutically active substances, for example, a mixture of a glucocortico-steroid with a bronchodilator (page 5, line 21 to page 6, line 10).

Where delivery by inhalation is desired, as much as possible of the proliposome powder of the present invention should consist of particles having a diameter of less than 10 microns, for example 0.01 to 10 microns or 0.1 to 5 microns (page 6, lines 27-30).

Bystrom also teaches that the proliposome powder of the present invention is useful for the local or systemic treatment of diseases and may be administered for example via the upper and lower respiratory tract. The proliposome powder for use in therapy, the use of the proliposome powder in the manufacture of a medicament for the treatment of diseases via the respiratory tract, and a method for the treatment of a patient in need of therapy, comprising administering to said patient a therapeutically effective amount of the said proliposome powder preparation. The proliposome powder preparation may be used in the treatment of inflammatory diseases in the respiratory tract, for example asthma, rhinitis, etc. Administration to the respiratory tract may be

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effected using a dry powder inhaler or a pressurized aerosol inhaler (page 9, line 15 to page 10, line 11).

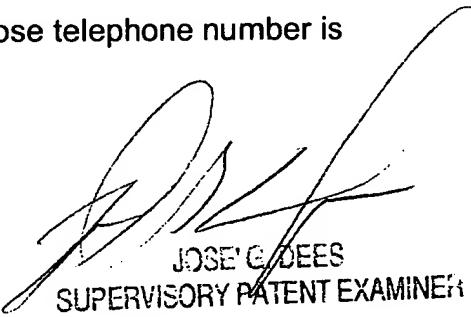
Although Bystrom does not specifically teach a combination product, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the preparations to a combined product because of the disclosed properties of the liposomes and their benefits in treating respiratory disorders and also the advantages of using liposomes as carriers for drug components.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
September 20, 2002


JOSE G. DEES
SUPERVISORY PATENT EXAMINER
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